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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,178	10/10/2003	Gerardo M. Castillo	017170-0008-999	2631
20583	7590	04/12/2007		
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			EXAMINER COVINGTON, RAYMOND K	
			ART UNIT	PAPER NUMBER
			1625	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		04/12/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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<b>Office Action Summary</b>	<b>Application No.</b> 10/684,178	<b>Applicant(s)</b> CASTILLO ET AL.	
	<b>Examiner</b> Raymond Covington	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2007.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 22,27,39 and 40 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22,27,39 and 40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10/10/07 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22, 27, 39 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing the deposition and buildup of A $\beta$  amyloid fibrils, it does not reasonably provide enablement for treating Alzheimer's disease. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The [eight] factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. The main issues are the correlation between clinical efficacy for Alzheimer's treatment and Applicants' amyloid binding assay.

a) Determining if any particular claimed compound would treat any particular disease would require synthesis of the compound, formulation into a suitable dosage form, and testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large quantity of experimentation. b) The direction concerning treating Alzheimer's disease is found in for example page 26 and examples 7, 8, 14 and 15 of the specification, which merely states Applicants' intention to do so. There is an assay described in examples 7 and 14 with no data but it is unclear if this assay is correlated to Alzheimer's disease. c) There is no working example of treatment of any disease in man or animals. The assay provides evidence that the present compounds affect the deposit and accumulation of amyloid fibrils. However, this does not demonstrate an Alzheimer's therapeutic effect. d) The nature of the invention is clinical treatment of Alzheimer's disease with procyanidin B2, which involves physiological activity. e) The state of the clinical arts is that there has been an ongoing scientific debate as to the importance of amyloid in the treatment of Alzheimer's disease. (see p. 26 spec.).

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors

involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). h) The scope of the claims involves treatment of many diseases via amyloid formation which includes hundreds of amyloid protein deposits embraced by the term amyloid. Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue

experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Applicants' remarks have been considered and are not persuasive.

Applicants in their response indicate that the compounds from the data have ‘potential’ use for effectively treating Alzheimer’s disease in a mammal. For the requirements of 35 USC 112 to be met the compound must ‘definitely’ inhibit/treat Alzheimer’s disease, ‘potential’ use is not enough.

While it is well settled that testing data, working examples are not needed to fulfill the requirements of 35 USC 112, it is also well settled that where compounds are alleged to be useful to treat a condition, that utility needs to be proved. In re Bergel and Stock (CCPA 1962) 130 USPQ 206. Further, allegations in the specification of utility that are or border on the incredible in light of contemporary knowledge in the particular art must be substantiated by acceptable evidence. Treating/inhibiting Alzheimer’s disease is sufficiently unusual to warrant substantiating evidence. Ex parte Busse et al (BPAI 1986) 1PQ2d. Currently, there is no umbrella compound that treats/inhibits Alzheimer’s disease as presently claimed.

Further regarding the Snow declaration of 2/1/06, it is noted that while screening and assay indicated that compounds encompassed by the claims have efficacy in inhibiting the formation, deposition, accumulation, or persistence of A $\beta$  amyloid fibrils in vitro, a symptom occurring in many diseases, does not necessarily have efficacy in treating the "cause" of the disease i.e. the disease per se. (see Cecil medical textbook p.1937-1938).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond Covington whose telephone number is (571) 272-0681. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie at telephone number (571) 272-0681.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair->

Art Unit: 1625

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contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Thomas McKenzie

SPE

Art Unit 1625



RKC